DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office
HFI-35 5142 PDC

60 8th Street, N.E.
Atlanta, Georgia 30309

December 11, 2000

VIA FEDERAL EXPRESS

Robert M. Kaminski
Chief Executive Officer
Leiner Health Products Inc.
901 East 233rd Street
Carson, California 90745

WARNING LETTER
(01-ATL-15)

Dear Mr. Kaminski:

An inspection of your drug manufacturing facility located at 4409 Northwest Airport Drive in Wilson, North Carolina, was conducted on November 6 - 17, 2000, by Investigators Kathleen D. Culver and Amy H. Ruble. The inspection revealed several significant deviations from the Current Good Manufacturing Practice for Finished Pharmaceuticals (CGMPs), as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 211. These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

You have failed to appropriately validate the manufacturing processes currently utilized for all of your drug products. You could not provide documented evidence which established a high degree of assurance that all of your manufacturing processes were effective and could consistently produce a product meeting its predetermined specifications and quality attributes.

Your facility has released [redacted] lots of 500 mg. acetaminophen film coated caplets that were manufactured utilizing a rework process that has not been appropriately validated. In addition, eight of these lots were released for packaging without sufficient stability data to support their labeled 36-month expiration date. Seven of these lots are currently in distribution channels with this unsubstantiated expiration date.

The Wilson facility manufactured [redacted] lots of pseudoephedrine hydrochloride 30 mg. tablets since November 1998 with an unvalidated process. Although this process was validated in 1994, the manufacturing process was significantly changed in November 1996 and not revalidated at that time, as it should have been. In February 2000 your firm attempted to

validate this process but failed to produce acceptable results. Although all of the process validation batches, and production batches made prior to the final conclusion of the validation study, were rejected. Your firm failed to appropriately respond to the finding that the process did not consistently produce uniform blend or tablets. The issue of product previously manufactured with this unvalidated process was ignored until the current FDA inspection.

The first six production batches of pseudoephedrine hydrochloride 60 mg. /chlorpheniramine maleate 4 mg. tablets were manufactured with a [redacted] minute final blending step instead of the [redacted] minute blend which had been validated. Your quality assurance department released two of these batches and one of these lots was commercially distributed. This lot (W0010089) was subjected to some additional testing for content uniformity but there was no documented rationale in the available records for the additional testing.

You have failed to provide adequate air filtration and air handling systems in critical manufacturing areas to include dispensing, granulation, and blending. Appropriate measures have not been taken to control recirculation of dust from production. Exhaust systems were not adequate to control dust and other contaminants in the production areas. White dust was noted to coat the stairs outside of room 146 which was being tracked into your general staging and warehouse area. White dust was also noted all over the floors, walls, surfaces and equipment in room 151 used primarily for the manufacture of naproxen sodium. On 11/7 a forklift was noted tracking dust from a blending room (#150) to the warehouse/staging area. The HVAC data for two air handling units indicated an air flow return rate of zero in room 146 (staging/dispensing) and room 152 (granulator #3).

You have failed to test stability samples at appropriate intervals to assess the stability characteristics of your drug products. A 325 mg. film coated aspirin lot with an expiration date of March 1999 was not tested until December 1999. Another lot of the same product with an expiration date of March 2000 was not tested until July 2000. Out-of-specification dissolution results were obtained for both lots when finally tested. Although a laboratory investigation was initiated, no further investigation was conducted since the product was beyond expiration date. A determination could not be made as to if these two lots continued to meet specifications throughout their labeled expiration date.

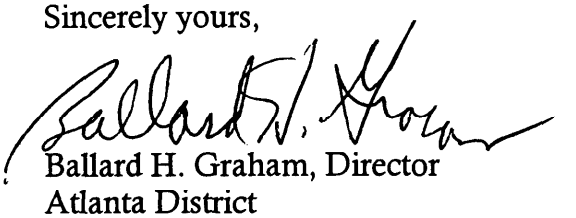
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The above deviations were included on the Inspectional Observations (FDA 483) which was issued to and discussed with Patrick Dunn, Senior Vice President for Quality & Regulatory Affairs, at the conclusion of the inspection. A copy of the FDA 483 is enclosed for your review. The specific violations noted in this letter and in the FDA 483 could be symptomatic of underlying problems in your firm's quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending New Drug Applications, Abbreviated New Drug Applications, or export approval requests may not be approved until the above violations are corrected. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory actions being initiated by the FDA without further notice. These actions include, but are not limited to seizure and/or injunction.

I am in receipt of a formal response to the FDA 483 that was presented to me during a meeting with Leiner corporate officials in Atlanta on December 8, 2000. We are encouraged by the corrective actions promised during this meeting. We also acknowledge that your firm has initiated several recalls in response to the observations made during the current inspection. We would hope that your response to this Warning Letter would include any steps undertaken to address the decision making processes which led to the problems noted during the inspection and resulted in violative products remaining in distribution unnecessarily.

Please notify this office in writing within fifteen (15) days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. You may reference the above December 8 response if you feel it adequately addresses the observations noted. Your response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely yours,



Ballard H. Graham, Director
Atlanta District

Enclosure

cc: Joseph Nolette, Plant Manager
Leiner Health Products Inc.
4409 Northwest Airport Drive
Wilson, North Carolina 27896